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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,463	07/01/2003	Francisco Cruz	67-97A	3099

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EXAMINER	
SOROUSH, LAYLA	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 06/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/612,463	CRUZ ET AL.	
	Examiner	Art Unit	
	Layla Soroush	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 7/1/03.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/25/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Priority

The Office Action is in response to the Preliminary Amendment filed July 1, 2003. This application is a DIV of 09/138,448 (PAT 6,630,515) which claims benefit of 60/057,385 08/28/1997. Claims 1-4 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what is meant by the terms "means for combining" of claim 1 and "means for transferring" of claim 4. The claims are rendered vague and indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al. (Temporal Parameters...– IDS) in view of Remmington.

Craft et al. teaches an I.ves administration of resiniferatoxin at a (0.33uM concentration. "The resiniferatoxin was dissolved in ethanol to which Tween-80 and saline were added (see page 480, Drugs)." The concentration limitation is met by the teachings of the reference.

Though, Craft et al. does not teach the use of a first and second container of the kit formulation, the employment of an I.V. instillation kit herein containing a unit dosage of the active compound and solvent in which resiniferatoxin is to be dissolved is considered obvious since the active compound is known to be useful in injection compositions containing the same solvents.

Remington teaches in IV fluid administration two container systems are common in the art. The primary IV fluid is used for purposes of keeping the vein open and can also serve as a vehicle for other drugs to be administered (an intravenous admixture — IV drip) and results in continuous blood levels of added drug (page 1545, left column, 1st paragraph). These fluids are commonly 50 or 100 mL Dextrose Injectjion, 5% or normal saline (page 1547, right column, 2nd paragraph). The Piggyback Method "refers to the intermittent intravenous drip of a second solution, the reconstituted drug, through the venipuncture site of an established primary IV system." This method eliminates the need for another venipuncture and also achieves drug dilution and peak blood levels within a relatively short time span. "Drug dilution helps to reduce irritation and early high serum levels an important consideration in serious infection requiring aggressive drug therapy (page 1546, right column, last paragraph)." The limitation "the means for

transferring an instillation dose of the therapeutic compound to a patient" of claim 4, is met by the teachings of Remington.

It would have been obvious to a person of ordinary skill in the art at the time of the invention was made to incorporate the composition into the claimed container. The incorporation would have been motivated by the teaching in Clark et al. that the composition of the formulation is administered by an I.ves apparatus; and further by Remmington that the intravenous drug administration apparatus allows for continuous mixing action within the vessel and further progressively diluting the secondary drug solution. Therefore the skilled artisan would have had a reasonable expectation of producing a diluted solution similar to the effect taught in the prior art reference.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blumberg (5,021,450 -- IDS) in view of Remmington.

Blumberg teaches desensitization by resiniferatoxin (RTX) can be activated by topical, intravenous, intraperitoneal, oral, and subcutaneous administration. The reference teaches RTX can be made into pharmaceutical compositions by combination with appropriate medical carriers or diluents. For example, suitable carriers include saline, polyethylene glycol, ethanol, sesame oil, cremophor, and isopropyl myristate. The compounds of the invention may be formulated into preparations for injections by dissolving, suspending, or emulsifying them in aqueous solvents such as normal saline. Additionally, the reference teaches in terms of composition, the compound of the

invention should be present between 0.0001 to 10% by weight, preferably 0.0001 to 1% by weight, the range limitations are met by the art teachings. The general teaching of the therapeutic compound renders the various phases (solution concentrate or dry powder) obvious. Blumburg teaches in Example 2, RTX in a 10% ethanol composition (column 12), as recited in claim 3.

Though, Blumberg does not expressively teach a first and second container of the kit formulation, the employment of an I.V. instillation kit herein containing a unit dosage of the active compound and solvent in which resiniferatoxin is to be dissolved is considered obvious since the active compound is known to be useful in injection compositions containing the same solvents.

Further, Remington teaches in IV fluid administration two container systems are common in the art. The primary IV fluid is used for purposes of keeping the vein open and can also serve as a vehicle for other drugs to be administered (an intravenous admixture—IV drip) and results in continuous blood levels of added drug (page 1545, left column, 1st paragraph). These fluids are commonly 50 or 100 mL Dextrose Injectjion, 5% or normal saline (page 1547, right column, 2nd paragraph). The Piggyback Method "refers to the intermittent intravenous drip of a second solution, the reconstituted drug, through the venipuncture site of an established primary IV system." This method eliminates the need for another venipuncture and also achieves drug dilution and peak blood levels within a relatively short time span. "Drug dilution helps to reduce irritation and early high serum levels an important consideration in serious infection requiring aggressive drug therapy (page 1546, right column, last paragraph)."

The limitation "the means for transferring an instillation dose of the therapeutic compound to a patient" of claim 4, is met by the teachings of Remington.

It would have been obvious to a person of ordinary skill in the art at the time of the invention was made to incorporate the composition into the claimed container. The incorporation would have been motivated by the teaching in Blumberg that the composition of the formulation is further diluted in saline; and further by Remmington that the intravenous drug administration apparatus allows for continuous mixing action within the vessel and further progressively diluting the secondary drug solution. Therefore the skilled artisan would have had a reasonable expectation of producing a diluted solution similar to the effect taught in the prior art reference.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7-9, 11, and 13 of U.S. Patent Application No. 09/138,448. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the co-pending application recites A method for alleviating symptoms of neurogenic urinary dysfunction comprising administering by intravesicular instillation to a human patient having said symptoms a therapeutically effective concentration in the range from 0.05 uM to 2.0 mM of a compound selected from the group resiniferatoxin, tinyatoxin, 20-homovanillyl-mezerein or 20-homovanillyl-12-deoxyphorbol-13-phenylacetate in a physiologically compatible solvent, said concentration being a concentration that does not cause meaningful burning or irritation to said patient, whereas the instant claims are A kit for intravesicular instillation comprising, a first container containing a unit dose of a therapeutic compound selected from the group resiniferatoxin, tinyatoxin, 20-homovanillyl-mezerein or 20-homovanillyl-12-deoxyphorbol-13-phenylacetate in a solution concentrate or dry powder form and a second container containing a physiologically compatible diluent capable of dissolving and maintaining in solution the therapeutic compound, the volume of said diluent being sufficient for intravesicular instillation of the unit dose and providing a concentration of the therapeutic compound of from 0.05 uM to 2.uM upon mixing the diluent with the therapeutic compound, and means for combining the diluent with the stock solution or lyophilized powder under sterile conditions. To one of ordinary skill in

the art it would be obvious to employ an I.V. instillation kit herein containing a unit dosage of the active compound and solvent in which resiniferatoxin is to be dissolved is considered obvious since the active compound is known to be useful in injection compositions containing the same solvents.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER